Amendments to the Specification

Please replace the paragraph beginning at page 1, line 14 with the following amended paragraph:

The skin (synonymously the cutis) is a protective membrane which covers the body and is composed of several layers including the epidermis and the cornium. A skin disorder is an anomaly or an abnormal skin growth and can appear at any cutis location, such as on a hand, foot [[of]] or face of a patient. Some skin disorders are more prevalent at pressure, wear or weight bearing locations, such as on the feet. A skin disorder can be a wart, bunion, callus, corn, ulcer, neuroma, hammertoe, dermatofibroma, keloid, mole (such as a typical mole or dysplastic nevi), granuloma (such as a pyogenic granuloma) and a keratose (such as a seborrheic keratose).

Please replace the paragraph beginning at page 2, line 1 with the following amended paragraph:

A callus is a protective cutis pad made up of a thickened upper layer of skin which forms due to repeated rubbing of the skin at that location. A corn is a small callus which develops on the top of the toes due to pressure or rubbing against shoes or other toes. A corn can also develop due to a hammertoe condition which is an abnormal contraction of buckling of the toe because of a partial or complete dislocation of one of the joints of the toe or the joint where the toe joins with the rest of the foot. As the toe becomes deformed, it can rub against a shoe and the resulting irritation can cause the build up of more and thicker skin (a corn) as a protective response at that cutis location.

Please replace the paragraph beginning at page 2, line 31 with the following amended paragraph:

A neuroma is a swelling or scarring of a small nerve that connects to two toes and provides sensation to these toes. Symptoms of a neuroma can include pain or numbness, usually affecting the third and fourth toes. Neuromas frequently start as a numbness or tenderness in the ball of the foot.

Please replace the paragraph beginning at page 20, line 1 with the following amended paragraph:

A method according to my invention can be carried out by administration of a Clostridial toxin to a patient with, or who is predisposed to, a skin disorder. The Clostridial toxin used is preferably a botulinum toxin (as either a complex or as a pure [i.e. about 150 kDa molecule], such as a botulinum toxin A, B, C, D, E, F or G. Administration of the Clostridial toxin can be by a transdermal route (i.e. by application of a Clostridial toxin in a cream, patch or lotion vehicle), subdermal route (i.e. subcutaneous or intramuscular) or intradermal route of administration.

Please replace the paragraph beginning at page 21, line 16 with the following amended paragraph:

The Clostridial neurotoxin is administered in a therapeutically effective amount to alleviate a symptom of a skin disorder. A suitable Clostridial neurotoxin may be a neurotoxin made by a bacterium, for example, the neurotoxin may be made from a *Clostridium botulinum*, *Clostridium butyricum*, or

Clostridium beratti. In certain embodiments of the invention, the skin disorder can be treated by applying to (topical) or into (intra or transdermal) the skin of a patient a botulinum toxin. The botulinum toxin can be a botulinum toxin type A, type B, type C1, type D, type E, type F, or type G. The skin disorder alleviating effects of the botulinum toxin may persist for between about 2 weeks (i.e. upon administration of a short acting botulinum toxin, such as a botulinum toxin type E) and 5 years (i.e. upon implantation of a controlled release botulinum toxin implant). The botulinum neurotoxin can be a recombinantly made botulinum ~~neurotoxins, such as botulinum toxins~~ neurotoxin, such as a botulinum toxin produced by an E. coli bacterium. In addition or alternatively, the botulinum neurotoxin can be a modified neurotoxin, that is a botulinum neurotoxin which has at least one of its amino acids deleted, modified or replaces, as compared to a native toxin or the modified botulinum neurotoxin can be a recombinant produced botulinum neurotoxin or a derivative or fragment thereof.

Please replace the paragraph beginning at page 22, line 20 with the following amended paragraph:

My invention also encompasses a method for treating a skin disorder by locally administering a botulinum toxin (such as a botulinum toxin type A, B, C, D, E, F or G, in an amount [[of]] from 1 unit to 3,000 units per treatment session) to a patient predisposed to experience a skin disorder, thereby preventing the patient from experiencing a skin disorder. A patient predisposed to a skin disorder is a human who has experienced a skin disorder at least once within the last twelve months. The local administration can be carried out by subcutaneous or by topical administration of the botulinum toxin at a location on

or within the skin of the patient where a skin disorder is located. The skin disorder can be reduced in size by from about 20% to 100%.

Please add the following new paragraphs after the paragraph beginning at page 22, line 20:

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 illustrates a mechanism of action of a botulinum toxin.

Please replace the paragraph beginning at page 28, line 23 with the following amended paragraph:

Furthermore, it has been demonstrated that denervation of the skin can cause the epidermis to [[began]] begin to degenerate or to become thinner. Hsie S., et al., *Modulation of kerationocyte proliferation by skin innervation,* J Invest Dermatol. 1999 Oct;113(4):579-86; Hsieh S., et al., *Epidermal denervation and its effects on keratinocytes and Langerhans cells,* J Neurocytol. 1996 Sep;25(9):513-24.); Chiang et al., *Regional difference in epidermal thinning after skin denervation, Exp Neurol* 1998 Nov;154(1):137-45; Li Y., et al., *Sensory and motor denervation influence epidermal thickness in rat foot glaborous skin,* Exp Neurol. 1997 Oct;147(2):452-62 (botulinum toxin blockade caused epidermal thickness to be significantly reduced in the central area of the sole of the rat foot).

Please replace the paragraph beginning at page 29, line 13 with the following amended paragraph:

The amount of the Clostridial toxin administered according to a method within the scope of the disclosed invention can vary according to the particular characteristics of the skin disorder being treated, including its severity and other various patient variables including size, weight, age, and responsiveness to therapy. To guide the practitioner, typically, no less than about 1 unit and no more than about 50 units of a botulinum toxin type A (such as BOTOX®) is administered per injection site (i.e., to each skin disorder location injected), per ~~patent~~ patient treatment session. For a botulinum toxin type A such as DYSPORT®, no less than about 2 units and no more than about 200 units of the botulinum toxin type A are administered per administration or injection site, per ~~patent~~ patient treatment session. For a botulinum toxin type B such as MYOBLOC®, no less than about 40 units and no more than about 2500 units of the botulinum toxin type B are administered per administer administration or injection site, per ~~patent~~ patient treatment session. Less than about 1, 2 or 40 units (of BOTOX®, DYSPORT®, and MYOBLOC® respectively) can fail to achieve a desired therapeutic effect, while more than about 50, 200 or 2500 units (of BOTOX®, DYSPORT® and MYOBLOC® respectively) can result in clinically observable and undesired muscle hypotonicity, weakness and/or paralysis.

Please replace the paragraph beginning at page 30, line 1 with the following amended paragraph:

More preferably: for BOTOX® no less than about 2 units and no more than about 20 units of a botulinum toxin type A; for DYSPORT® no less than about 4 units and no more than about 100 units, and; for MYOBLOC®, no less than about 80 units and no

more than about 1000 units are, respectively, administered per injection site, per ~~patent~~ patient treatment session.

Please replace the paragraph beginning at page 30, line 9 with the following amended paragraph:

Most preferably: for BOTOX® no less than about 5 units and no more than about 15 units of a botulinum toxin type A; for DYSPORT® no less than about 20 units and no more than about 75 units, and; for MYOBLOC®, no less than about 200 units and no more than about 750 units are, respectively, administered per injection site, per ~~patent~~ patient treatment session. It is important to note that there can be multiple injection sites (i.e., a pattern of injections) for each patient treatment session.

Please replace the paragraph beginning at page 37, line 3 with the following amended paragraph:

A 61 year old diabetic female presents with a pain that has developed at the bottom of her heel, and it has gotten worse. The patient is not aware of having had any injury that caused it. The patient is diagnosed with a painful bone spur at the center of the left heel. She reports a dull ache most of the time, but when the patient first gets out of the bed in the morning, or when getting up after sitting for a period of time during the day, the pain in the heel is almost unbearable, ~~felling~~ feeling like the heel has been bruised, from falling on a rock barefoot, but it is worse. Several therapies including topical lidocaine, NSAIDS, and therapy are tried with little relief. Surgery is not an option due to the poor blood circulation of the patient's lower limbs. Therefore, botulinum

toxin type A as 30 units total can be applied following use of a topical anesthetic, 10U/site in three subcutaneous injection sites spaced evenly apart over the painful area. On follow-up 2 weeks later, the patient can report significant relief of pain and can tolerate walking. Four weeks later the patient can ~~reported~~ report no pain and be able to tolerate walking greater distances than two weeks earlier.

Please replace the paragraph beginning at page 380, line 9 with the following amended paragraph:

A 48 year old female presents with a history of genital warts. Examination of the patient reveals six flesh-colored bumps or tiny, cauliflower-like maculopapular warts of various sizes (0.05 cm^2 to 2 cm^2). The patient had been treated with several different treatment methods; direct application of bleomycin, acetylsilic acid, with little or no relief. The patient refuses laser or other types of invasive methods of treatments. A botulinum toxin type A is applied directly into the wart areas via intra-dermal injection, in an effective amount of, but not limited to 5U/cm^2, for a total of 30U. Upon follow up 4 weeks later, 3 of the smaller warts, can ~~have disappered~~ disappear completely and at 2 months, the patient can report disappearance of the remaining warts.

Please replace the paragraph beginning at page 38, line 23 with the following amended paragraph:

A 54 year old male has a history of painful plantar warts and returns to the clinic following an exacerbation of wart growth on the plantar region of his right foot. Upon examination, 3 various sized warts (1 cm^2, 2.5 cm^2 and 4.4 cm^2),

with a rubor colored ring surrounding 2 of the 3 warts, ~~suggesting inflammation. Patient has tried in bleomycin~~ suggests inflammation. The patient has tried bleomycin but relief was minimal and caused significant pain following injection. Therefore, a botulinum neurotoxin is considered as an alternative and 5U/cm^2 can be applied in a topical formulation directly to the wart for a total of 45 U. On follow up 2 months later, the patient can report complete relief of pain and upon examination, there were no signs of inflammation (rubor rings not present), and 2 of the 3 warts had disappeared completely with only ~ 1 cm^2 of the 4.4 cm^2 wart visible.

Please replace the paragraph beginning at page 39, line 4 with the following amended paragraph:

In each of the examples above a botulinum toxin type B, C, D, E, F or G can be substituted for the botulinum toxin type A used above, for example by use of 250 units of a botulinum toxin type B. The specific amount of a botulinum toxin (such as BOTOX®) administered depends upon a variety of factors to be weighed and considered within the discretion of the attending physician and in each of the examples insignificant amounts of botulinum toxin ~~enter~~ appear systemically with no significant side effects.